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How effective is periarticular drug infiltration in providing pain relief and early functional outcome following total hip arthroplasty?

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ABSTRACT

The aim of the study was to compare the efficacy of periarticular injection of a cocktail of analgesic drugs (PIC) with epidural infiltration (EA), in providing postoperative pain relief and early functional improvement following Total Hip Arthroplasty (THA).

Methods: 50 patients undergoing unilateral THA were randomized to receive either EA or PIC for postoperative pain control. Postoperative pain relief, as determined by the visual analogue scale (VAS), functional recovery and side effects related to EA and PIC were assessed.

Results: PIC resulted in significantly lower VAS scores [0.48(0.71) vs 3.04(2.07)] in the first 24 h after surgery [mean (SD)], when compared to EA. The pain relief continued to be significantly lower even on the 10th postoperative day. Functional recovery was significantly better in the PIC group, with patients being able to walk longer distances and climb steps more quickly following THA. EA, unlike PIC was associated with side effects like nausea, vomiting, motor weakness, back pain and urinary retention. The overall satisfaction rate with treatment was significantly better in PIC group (9.04/10) than those who received EA (7.76/10).

Conclusion: PIC provides significantly better pain control and functional recovery in the early postoperative period, with less side effects when compared with EA. PIC should be the choice for pain control following THA.

1. Introduction

Total Hip arthroplasty (THA) is one of the most successful surgical treatments that can be offered to patients with end-stage hip arthritis. Early rehabilitation after total hip arthroplasty leads to better patient satisfaction and better outcomes – both subjective and objective.[1] One of the most important factors restricting early mobilization following THA is post-operative pain.[2,3] It has been shown that severe postoperative pain translates to poor short and medium term outcomes. Further, upto 28.1% of these patients continue to have chronic pain.[4,5] Even though myriad options are available for post-operative pain relief, the most widely used modality is Epidural Analgesia (EA).[6] EA, when compared with general anesthesia is associated with longer periods of pain relief, lower intraoperative blood loss, shorter duration of surgery, reduction in perioperative and postoperative transfusion requirements and a lower rate of deep vein thrombosis.[7] However the benefits of epidural analgesia must be weighed against its potential complications such as urinary retention, hypotension, pruritus, and motor deficits that may delay mobilization.[8,9] It is an invasive procedure and necessitates restricting the patient's mobility till the epidural lines are removed. The use of multimodal pain control combined with Periarticular Infiltration of Analgesic Cocktail (PIC) is an alternative to EA in THA.Multiple studies have shownthat periarticular infiltration using multimodal drugs can reduce the postoperative analgesia requirements and duration of hospitalization.[10–12] We hypothesized that PIC leads to lower

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postoperative pain, faster recovery, less opioid consumption and better patient satisfaction, when compared to EA.

The purpose of this study was to assess the efficacy of PIC, in terms of effective pain control and early rehabilitation following THA. This was done by comparing the efficacy and complications with the current method of postoperative pain control used at our institution i.e. epidural analgesia.

2. Methods

This was a two arm, parallel, prospectiverandomized controlled trial. The trial was registered with the Central Trial Registry of India (CTRI) (Registration no-CTRI/2017/10/010071) as a randomized controlled trial titled "How effective is periarticular drug infiltration in providing pain relief following Total Hip Arthroplasty?" After obtaining approval from our institutional review board, with written informed consent, patients were randomized to two groups. This study was conducted as a single center study, involving the surgeons who werespecialized in hip surgery.

Patients undergoing unilateral uncemented THA were recruited for the study. They were excluded if they were more than 80 years of age; had a history of cardiovascular disease; undergoing complex primary or revision arthroplasty or if the opposite hip was also extremely painful.

Patients were randomized into two arms by block randomization with concealed envelope method. In the EA group, an epidural catheter was placed at the L2-L3 or L3-L4 level. The catheter was connected to an infusion pump delivering continuous infusion with 0.1% Bupivacaine and 2mcg/ml of Fentanyl at 4–6 ml per hour for 48 h postoperatively. They were excluded if satisfactory epidural accesses could not be achieved. The second group receivedperiarticular infiltration of an analgesic cocktail of drugs. The analgesic cocktail consisted of 50 ml of 0.2% Ropivacaine, 10 ml Normal saline, 40 mg Methylprednisolone acetate, 10 mg Morphine, 30 mg Ketorolac, and 1gm Cefazolin. The cocktail was injected intothe capsule before the femoral stem was inserted – 10 ml inferiorly, 10 ml anteriorly, and another 10 ml posteriorly - around the rim of the acetabulum. Following reduction of the femoral head, the gluteus medius, gluteus maximus, tensor fascia lata and iliotibial band were injected sequentially with the rest of the cocktail.

All patients received peri-operative analgesia with 100 mg of Aceclofenac, 20 mg of Omeprazole and 75 mg of Pregabalin every 12 h– all started 36 h before the surgery.Postoperatively all patients received Inj. Paracetamol 1gm intravenously, once every 6 h for 48 h, followed by Tab. Paracetamol 1gm once every 6 h for 5 days. Injection Morphine 5 mg (subcutaneous) was given as required for breakthrough pain in the immediate postoperative period. Those on EA had either bolus doses or an increase in the infusion rate for breakthrough pain. Intravenous Ondansetron 4–8 mg was used for postoperative nausea and vomiting.

Surgery was performed under general anesthesia or spinal anesthesia using a modified Hardinge anterolateral approach in the lateral position. Prostheses used were either a combination of a Corailstem (DePuySynthes Joint Reconstruction, Cedex, France) and Pinnaclecup (DePuySynthes Joint Reconstruction, Warsaw, USA) or an R3cup and Polar or Synergy stem (Smith & Nephew, Memphis, USA). The implants were all uncemented. A closed suction drain was placed under the iliotibial band before wound closure and removed 36 h later. Tranexamic acid (10–15 mg/kg) was injected intravenously 15 min before skin incision, and two further doses were given 3 and 6 h later. Anticoagulation therapy was initiated as per institutional guidelines.

Patients underwent a standardized physiotherapy programme that involved foot and calf pump exercises in bed and sitting on the day of surgery. They were encouraged to walk from the second postoperative day with the aid of a walker. The distance walked at the first attempt was noted. The number of days taken to walk 100 m and to climb a flight of 14 steps was documented. The distance covered in 6 min with a walker was recorded on the 10th postoperative day. The duration of inpatient stay was not considered, as several patients opted to continue as in inpatient till suture removal.

Pain experienced by the patient postoperatively was assessed using the Visual Analogue Scale (VAS) by the primary investigator on a daily basis. The patients were asked to score their pain from 0, representing no pain, to 10 for maximum pain. The pain score was also recorded every 4 h by the hospital pain team for the first 72 h. The pain team was blinded, as they were not aware of the ongoing study. The maximum VAS score for each day was noted. Additional medication used for breakthrough pain was noted.

Side effects like nausea, vomiting, pruritis, headache, urinary retention, back pain, cardiovascular complications, infection, postoperative wound ooze, ICU stay, nerve palsy, and mortality were noted.

On the 10thpostoperative day, the patients were asked to give a score for their overall satisfaction with their procedure, and this was scored on a scale from 1-10.

3. Statistical analysis

Based on the study by Hofstad et al the median pain score on mobilization on the first post operative day on a 10 point Likert scale, was about 4 (3–5).[13] Keeping the non-inferiority margin at 1.5 with alpha and beta errors at 5% and 20% respectively, the sample size needed minimum was 12 subjects in each arm. We decided to study 25 subjects in each arm.

Data was entered using EPIDATA software. Data was screened for outliers and extreme values using Box-Cox plot and histogram. All baseline variables were expressed in terms of mean and SD. All categorical variables were reported using frequencies and percentages. Chi-square test was performed between categorical risk variables. T- tests were performed between the groups for continuous variablesif the outcome variable distribution was normal, otherwise a Mann Whitney U test was done. Differences were considered significant at $p < 0.05$. All the statistical analysis was performed using SPSS 21.0

4. Results

During the period of study, we performed 104 primary THAs. 58patients satisfied the inclusion criteria and were randomized for the study.Five patients who were randomized for EA were excluded from the study because of failure to get a satisfactory epidural accesses determined by the senior anaesthetist on the case and another three patients were excluded as they hadintraoperative complications that restricted postoperative mobilization. A total of 50 patients participated in the study, of which 25 were randomized to receive the PIC and 25 received EA (Fig. 1). Patient demographic data is summarized in Table 1.

The preoperative VAS score (0–10) was similar for both groups: 5.96(1.21) for PICand 5.88(1.42) for EA [mean (SD)].Patients who received PIChad significantly lower VAS scores as compared to those who received EA: [0.48(0.71) vs 3.04(2.07)] in the first 24 h after surgery ($p < 0.001$). Pain scores remained significantly lower in the PIC group than the EA group [1.00(0.58) vs2.24(0.97)] on the third postoperative day ($p < 0.001$) and even at review on the 10thpost operative day [0.92(0.57) vs1.96 (0.89)] ($p < 0.001$) (Fig. 2).

Functional recoveryfollowing surgery was significantly better in thePIC group when compared to those who received EA. The mean walking distance on the 3rd post op day was 63.60(38.09)

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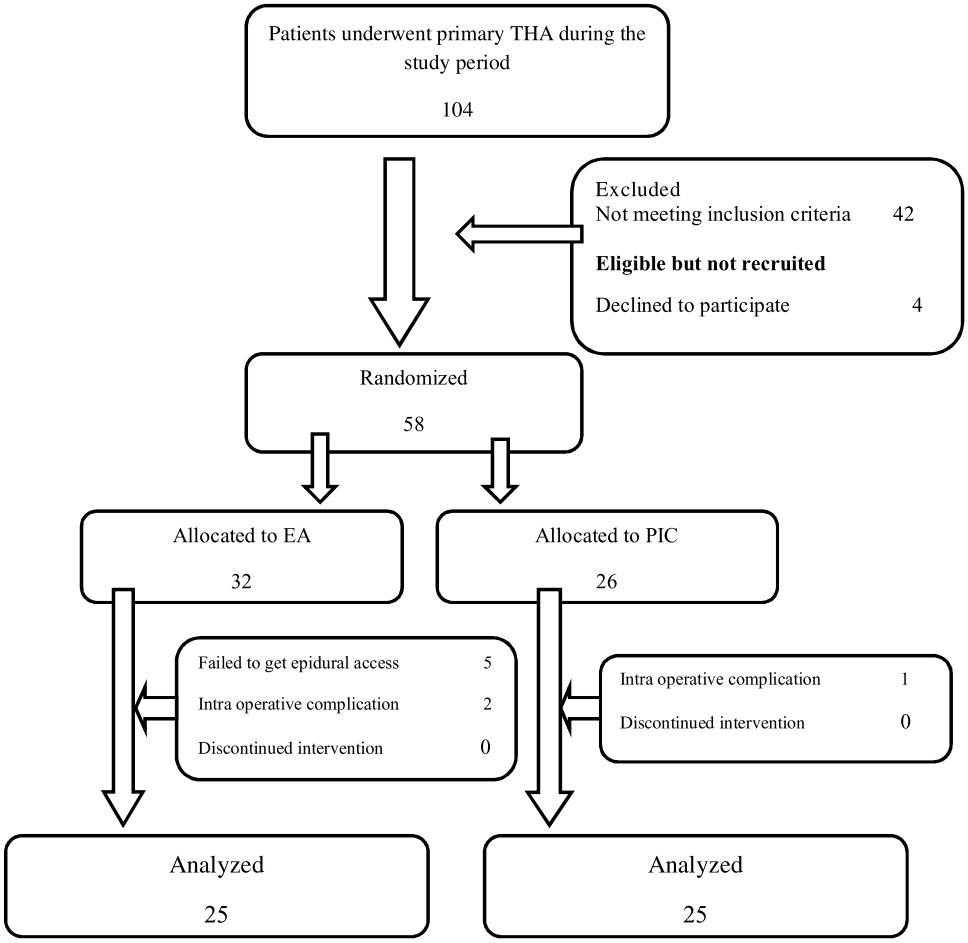

Fig. 1. Consolidated Standards of Reporting Trials diagram showing the flow of patients through the study.

metersfor those who received PIC, as opposed to 25.72(26.23) meters for those who received EA($p < 0.001$).Subsequent functional improvement was also consistently better in the PIC group when compared to the EA group, as reflected by the number of days taken to climb 14 steps [4.96(1.10) vs 6.28 (1.72)days], number of days taken to walk a distance of 100 m [4.32(1.31) vs 5.84(1.82) days] and the distance walked on the 10th postoperative day [154.60(35.99)vs 127.24(46.36) meters] (Table 2).

Table 1
Patient demographics and baseline clinical characteristics.

Patient characteristics	PIC	EA	**p-value**
Age [mean (SD)]	41.32 (10.84)	43.32 (13.04)	0.558
Sex (Male/Female)	17/8	16/9	0.765
BMI (Kg/m^2) [mean (SD)]	23.95(4.85)	26.20(5.75)	0.140
ASA (I/II)	12/13	12/13	1.00
Preoperative VAS score [mean (SD)]	5.96 (1.21)	5.88 (1.42)	0.831
Side Right/Left	15/10	12/13	0.395
Diagnosis AVN	5	11	
AS	13	5	
RA	1	2	
Fracture NOF	2	3	
Primary OA	1	0	
Displastic	0	2	
Perthes sequelae	2	0	
Post traumatic	0	1	
Post infective	1	1	
Implant Corail / Pinnacle	14	18	
R3/Polar/Synergy	11	7	

SD-Standard Deviation, AVN-Avascular Necrosis, AS-Ankylosing Spondylitis, RA-Rheumatoid Arthritis, NOF-Neck of Femur, OA-Osteoarthristis.

Patients who received EA for postoperativepain relief had more adverse events. In the EA group, three patients had urinary retention that required catheterization, two patients had more than 2 episodes of vomiting, three patients had bilateral lower limb paresthesia that recovered once the epidural infusion was

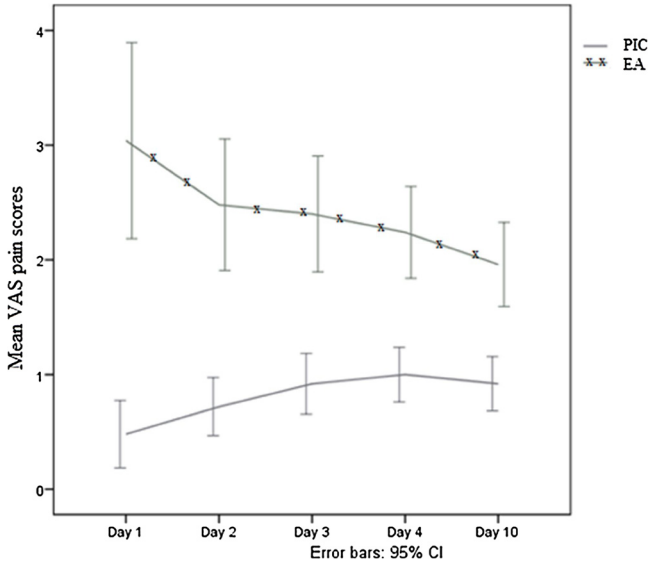

Fig. 2. Mean postoperative VAS scores for patients receiving PIC and EA. Legend: Error bars represent 95% confidence interval.

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Table 2
Post-operative functional outcome.

Functional outcome	PIC	EA	p-value
Distance walked on 3rd post op day (Meters) [mean (SD)]	63.60 (38.09)	25.72 (26.23)	0.001
Number of days taken to walk 100 meters [mean (SD)]	4.32 (1.31)	5.84 (1.82)	0.002
Number of days taken to climb 14 steps [mean (SD)]	4.96 (1.10)	6.28 (1.72)	0.002
Distance walked in 6 minutes on the 10th post op day (Meters)[mean (SD)]	154.60 (35.99)	127.24 (46.36)	0.024
Mean satisfaction score on 10th post op day (1–10) [mean (SD)]	9.04 (0.54)	7.76 (0.52)	<0.001

stopped and one patient had persistent back pain.Two patient in EA group required top up of epidural infusion and one required supplemental opioid (morphine) injectionfor pain relief. Among those who received PIC for postoperative pain control, onepatient developedpostoperative urinary retention requiring catheterization. There were no other adverse events documented for these patients (Table 3). The overall satisfaction rate with treatment on a scale of 1–10, was significantly better in those who received PIC [9.04(0.54)]when compared to those who received epidural anesthesia for pain control [7.76(0.52)].

5. Discussion

One of the prerequisites for accelerated recovery following THA is optimal pain relief following surgery.[14] Too often, patients are given analgesic medications only after the onset of pain. It is now well recognized that regular"round the clock" administration of pain medications is more effective at alleviating pain than the previous protocol of "analgesia on demand".[15]

A better understanding of the complexity of pain perception has led to the development of multimodal analgesia, which targets additional aspects of pain perception not addressed by narcotic medications.[16] Pre-emptive analgesia with drugs likepregabalin, and NSAIDs have helped reduce the severity of postoperative pain.

With EA for postoperative pain control, many patients encounter side effects like postoperative hypotension, urine retention and bowel dysfunction, prolonged sensory or motor deficitsandoccasionally have adverse reactions to the opiods in the infusion including nausea, vomiting, pruritis, drowsiness, and respiratory depression.[16,17] EA also necesitates the use of an epidural catheter and syringe pump, which limits patient mobilisation.

Peri capsular injections use a combination of different analgesics. Local anesthetics are the basic ingredient in most cocktail injections and they reduce pain by blocking voltage-gated sodium channels in the pain pathway. Nonsteroidal anti-inflammatory agents and corticosteroids block peripheral production of inflammatory mediators and desensitize the nociceptors. Opioid receptors are present in lower densities peripherally as compared with the central nervous system, but their inclusion in injections has been shown to improve pain relief.[18] Synergistic effects of this multimodal approach help to reduce the use of conventional opioid analgesics and to allow early mobilization.[19]

Table 3
Complications following PIC and EA.

Complications	PIC	EA
Nausea/Vomiting	0	2
Urinary Retention	1	3
Motor Neuropraxia	0	3
Extra Morphine doses	0	3
Back pain	0	1

The primary objective of this study was to compare the effectiveness of PIC and EA in providing pain relief following THA and to compare the functional recovery, and the profile ofadverse effectsin the two groups. The PIC group had significantly lower pain score when compared with the EA group during the first 10 days of surgery. This difference was most pronounced in the immediate postoperative period and continued even up to the 10thpost-operative day. Though the half-life of ropivacaine is only 4 h,[20] the prolonged "analgesic" benefit of the cocktail could be due to a variety of factors. It is possible that since the acute postoperative pain is suppressed due to the analgesic effect of ropivucaine, the "centralization of pain" that normally occurs following painful stimuli is mitigated.[21] Steroids are known to have an analgesic effect and this could have an additive effect. The use of local morphine in the capsular and muscle tissue too helps in lowering the pain for significantly prolongedperiods.

Functional recovery in the post-operative period was significantly better with PIC. Patientswere able to walk longer distances and were able to climb steps sooner following the use of PIC, when compared to those that had EA. Overall satisfaction following THA was significantly better in those who received PIC. EA was also associated with considerable adverseeffects like nausea, vomiting and urinary retention. From the above observations, one can conclude that the use of periarticular injection of the analgesic cocktail for pain relief resulted in superior outcomes when compared to EA.

There are few studies on the effectiveness of periarticular injection of analgesic cocktail with conflicting conclusions.[10,11,22,23] Parvataneniet al in their prospective randomized study compared the effectiveness of periarticular injections with patient-controlled analgesia. The periarticular injections group demonstrated significantly lower pain scores and higher overall satisfaction than the patient-controlled analgesia group. They concluded that periarticular injection with a multimodal protocol is safe and provides excellent pain relief and functional recovery, and that periarticular injection can replacethe conventional pain control modalities.[10] Kerr and Kohan reported on local infiltration analgesia with a mixture of ropivacaine, ketorolac, and adrenaline into the tissues around the surgical fieldand concluded that it is a simple, practical, safe, and effective for pain management after knee and hip surgery.[24]

The evidence is however not indisputable. Jules-Elysee et al conducted a randomized study of 84 patients, with one arm receiving patient controlled epidural analgesia, and the other arm receiving pericapsular injections. While the side effects were more with the epidural group, the pain score and functional improvement following surgery and time to discharge were no better in the PIC group, infactopioid consumption for breakthrough pain was more in the PIC group.[25] Hofstad and colleagues after their placebo controlled randomized double blinded trial concluded that local infiltration ofropivacaine did not provide any extra analgesic effect after THA, as compared to placebo. They concluded that the pain control was mainly due to the use of the preoperative and postoperative multimodal analgesic regimen.[13] Solovyova et al

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found that periarticular injection did not do any better than acontinuous infusion of saline in terms of pain control.[26]

However, other studies have had results similar to our study. Pandazi et al showed that periarticular infiltration was clearly superior to PCA (Patient controlled analgesia) with morphine after THA, providing better pain relief and lower opioid consumption postoperatively.[27] Kuchalik et al while comparing PIC with intrathecal morphine found that lower pain scores in the immediate postoperative period in those who received intrathecalmorphine. However subsequently, analgesic consumption, pain on mobilization, and side-effects were lower in patients receiving PIA.[28] They concluded that PIC is a better option for pain control in patients undergoing THA. Murphy et al conducted a randomized study with PIC and placebo for pain control and demonstrated that periarticular injection can supplement available postoperative analgesic techniques and reduce postoperative morphine requirements after THA.[29] A meta-analysis by Wang et al of 666 patients from 8 different randomized control trials concluded that the periarticular injection group had better pain relief at rest, less opioid consumption, and less length of hospital, when compared with the placebo group ($P < 0.05$). They however noted no significant differences in activity related visual analogue score and complications between the 2 groups.[12]

In our study, since both groups had similar preoperative and postoperative protocols, the differences in outcome could be inferred to be exclusively dependent on the type of perioperative analgesia used. It should be notedhowever, that the epidural catheter placement was done by anaesthesiologists with varying skill and experience, while the PIC was given by the primary surgeon. This could have had a bearing on the relatively poor analgesic effect of EA. The incidence of the complications associated with EA is influenced by the dose, volume and use of bolus delivery of drugs- which in-turn is directly influenced by the experience and understanding of the anaesthesiologist. However, this study is a reflection of the current practice followed in our institution, and hence reflectsground reality.We, therefore conclude that periarticular injection of a cocktail of drugs is more effective than epidural analgesia in providing pain relief and early functional recovery, and we suggest that it should be considered as the analgesia of choice for unilateral total hip replacement.

Conflict of interest

None.

We state that the paper is not based on previous communication to a society or meeting

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Catogory of study

Randomised clincial trial.

Central Trial Registry of India (CTRI) Registration no-CTRI/2017/10/010071.

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